PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 5 :		(11) International Publication Number:	WO 93/03669
A61B 5/04	A1	(43) International Publication Date:	4 March 1993 (04.03.93)

(21) International Application Number: PCT/US92/06967

(22) International Filing Date: 26 August 1992 (26.08.92)

(30) Priority data:
742,719 26 August 1991 (26.08.91) US

(71) Applicant: PERINATRONICS MEDICAL SYSTEMS, INC. [US/US]; 2411 Crofton Lane, Suite 14B, Crofton, MD 21114 (US).

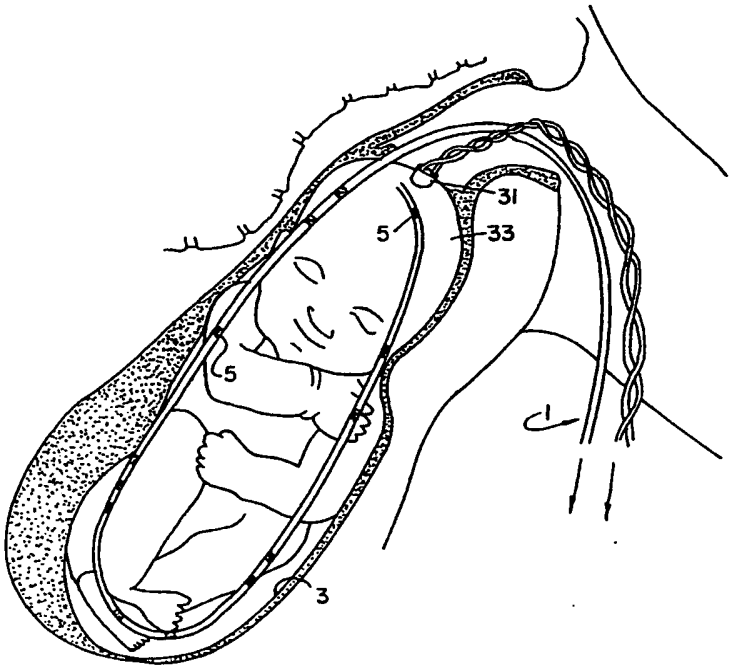
(72) Inventors: FRANK, Thomas, H. ; 1703 Peartree Lane, Crofton, MD 21114 (US). BLAUMANIS, Otis, R. ; 16201 Yeoho Road, Sparks, MD 21152 (US).

(74) Agent: WRAY, James, C.; 1493 Chain Bridge Road, Suite 300, McLean, VA 22101 (US).

(81) Designated States: AU, CA, JP, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: INTRAUTERINE ELECTRODE ARRAY FOR THE DETERMINATION OF FHR



(57) Abstract

The invention relates to an elongated intrauterine electrode array that is not attached directly to the fetal scalp and can derive a fetal ECG signal indicating the fetal heart rate and beat-to-beat variability data. The invention has a mylar ribbon with copper track conductors on the ribbon, terminators connected to the conductors, and electrodes connected to the conductors at various locations for receiving the material and fetal ECG signals. The electrodes are gold-plated and spherical. The electrodes and conductors are embedded in a silicone coating and the electrodes are placed on opposite sides of the array.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria
AU	Australia
BB	Barbados
BE	Belgium
BF	Burkina Faso
BG	Bulgaria
BJ	Benin
BR	Brazil
CA	Canada
CF	Central African Republic
CG	Congo
CH	Switzerland
CI	Côte d'Ivoire
CM	Cameroon
CS	Czechoslovakia
CZ	Czech Republic
DE	Germany
DK	Denmark
ES	Spain
FI	Finland
FR	France
GA	Gabon
GB	United Kingdom
GN	Guinea
GR	Greece
HU	Hungary
IE	Ireland
IT	Italy
JP	Japan
KP	Democratic People's Republic of Korea
KR	Republic of Korea
LI	Liechtenstein
LK	Sri Lanka
LU	Luxembourg
MC	Monaco
MG	Madagascar
ML	Mali
MN	Mongolia
MR	Mauritania
MW	Malawi
NL	Netherlands
NO	Norway
NZ	New Zealand
PL	Poland
PT	Portugal
RO	Romania
RU	Russian Federation
SD	Sudan
SE	Sweden
SK	Slovak Republic
SN	Senegal
SU	Soviet Union
TD	Chad
TG	Togo
UA	Ukraine
US	United States of America

1. INTRAUTERINE ELECTRODE ARRAY FOR THE DETERMINATION OF FHR

2. BACKGROUND OF THE INVENTION

a.) Field of the Invention

This invention is an intrauterine electrode array that is not attached directly to the fetal scalp at labor and delivery, from which one can derive a fetal ECG signal to obtain the fetal heart rate (FHR). The invention is capable of reliably recording the fetal and maternal ECG signals and processing these signals to obtain an accurate record of FHR and FHR beat-to-beat variability.

The device is useful in that it can successfully derive and reliably obtain the fetal heart rate by an intrauterine electrode array. This device will replace the objectionable and invasive spiral scalp electrode for routine use in fetal monitoring.

Continuous monitoring of the fetal heart rate during labor is the most widely applied adjunct to intrapartum assessment and care. Technological refinements over the past 15 years have led to the ability to predict a deteriorating fetal status at a time and under circumstances where prompt intervention can prevent fetal mortality and morbidity. Indeed, many clinicians feel that consistent use of electronic fetal monitoring is a primary factor in the relatively low incidence of intrapartum deaths and neonatal problems in this country. Although there may be valid questions regarding the validity of this belief, fetal monitoring seems entrenched as a routine procedure (Luthy et.al., 1987).

Undoubtedly, future progress in this field will be driven by technological as well as ethical and medicolegal considerations.

b.) Description of the Prior Art

The most popular and still the "gold standard" method of fetal monitoring involves the use of the so-called spiral or scalp electrode (Hon et.al.,1972). This is an invasive technique which requires the direct attachment of an electrode to the fetal scalp after rupture of the membranes. It is clearly not ideal and is associated with a number of potential complications (Goldkrand, 1982, Turbeville and McCaffree 1979, Sola, et.al., 1980, Okada,et.al., 1977, McGregor and McFarren, 1989). Although the technique is accurate, recent attempts to mechanically improve its application attest to its inherent 'inelegance' and cumbersome nature (Fukushima et.al., 1991).

Other, decidedly noninvasive techniques for FHR monitoring include phonocardiography (auscultation), external abdominal fetal ECG recording using standard ECG electrodes, and Doppler ultrasound (Lowensohn, 1976). Although phonocardiography may be useful in some circumstances, it cannot provide beat-to-beat variability data, an important parameter in fetal assessment. Doppler ultrasound technology has improved to the point where it offers some dependability in fetal monitoring during labor. However, it too suffers from an intrinsic inability to reliably detect beat-to-beat variability in FHR. The signal is derived from a complex of several cardiac mechanical events, which in effect conspire to introduce a quite artificial 'variability'

signal where there may be none.

From our perspective, the most promising approach to reliable and accurate FHR monitoring has been the external recording of fetal ECG using maternal abdominal electrodes. The major problems with this technique are the inevitable interference of the maternal ECG and random muscle noise. The maternal ECG contamination problem was solved by application of sophisticated signal processing including an adaptive digital filtering (cancellation) algorithm (U.S. Serial No. 61,575). Muscle noise remains as a potential problem.

The greatest obstacle to successful FHR monitoring by external ECG electrodes is related to poorly understood amniotic and physiologic factors which prevent the adequate recording of a fetal signal even after the maternal ECG and muscle noise contamination have been accounted for. There exists a curious condition of the fetal and maternal amniotic and physiologic parameters at gestation ages between 32 and 36 weeks during which it seems impossible to record a fetal ECG with external electrodes (van Bemmel, 1974). Since multiple electrode placements and the use of state-of-the-art electronics have failed to produce reliable recordings, one is tempted to invoke a virtual impotency principle, whereby accurate and reliable recording is simply not possible with external electrodes.

We have, therefore, on the one hand, an accurate but invasive, cumbersome and otherwise undesirable method, the scalp electrode. On the other hand, our previous efforts have resulted in accurate and reliable FHR monitoring using external electrodes and sophisticated signal processing. But the latter is not

always successful. Thus, there exists a need to reach a middle-ground, whereby the previously demonstrated power of our signal processing technology can be brought to bear on signals derived from noninvasive or minimally invasive intrauterine probes.

This invention offers an alternative approach - a multi-electrode array, to be inserted into the uterus after membrane rupture - a device which is not invasive to the fetus but which is compatible with the powerful signal processing capabilities already achieved (U.S. Serial 61,575). We have found reports of several attempts to derive a fetal ECG using an intrauterine probe. In 1988 a British group reported that an intrauterine electrode device was used to record FECG signals that ranged in amplitude from noise to 4-6 times the amplitudes recorded even with the scalp electrode (Randall, et.al., 1988). Nevertheless, this group was not able to take advantage of the large signal amplitude because of the maternal ECG contamination problem. In 1989 a Group at USC reported that using electrodes spaced along an intrauterine pressure device produced fetal ECG signals ranging from 20-375 microvolts but they were able to obtain fetal heart rate tracings in 60% of the cases (Strong, 1989). In 1991 Strong used an intrauterine probe of his own design to record the single combined fetal and maternal ECG signals. To remove the competing maternal ECG signal from this combined signal they utilized an adaptive noise cancelling technique which transformed maternal chest ECG derived signals to match the maternal ECG components found in the probe-electrode signal. They did not appreciate that these maternal only ECG signals could also be

obtained from our intrauterine electrode array.

U.S. Serial No. 61,575 describes the development of a noninvasive diagnostic instrumentation to determine instantaneous fetal heart rate, and FHR beat-to-beat variability (BBV) through the use of adaptive cancellation in electrocardiography. Preliminary data suggests that in using this instrumentation a reliable and accurate measure of FHR beat-to-beat variability can be made noninvasively during the third trimester of pregnancy. This apparatus implemented and evaluated novel adaptive electrocardiographic digital signal processing techniques that offer potential diagnostic and monitoring value in the field of fetal heart rate monitoring. This instrumentation technique, as previously developed, is capable of obtaining accurate records of FHR and BBV noninvasively from ECG electrodes which collect both maternal thoracic and abdominal ECG signals.

Two significant advances in instrumentation were achieved in prior work. First, a signal conditioning and amplification system was developed that reduces electronic and 60 Hz power line interference to within 1-2 uV; far below that required for conventional electrocardiography. Second, an electrocardiographic Adaptive Digital Filter was developed. The ADF optimizes a set of adaptive cancellation algorithms for the cancellation of the maternal ECG components of an abdominal ECG signal in order to calculate instantaneous FHR. We have completed the biomedical engineering development and initial clinical testing of the hardware and microprocessor software algorithms for this processor. This instrumentation can

adaptively cancel the maternal ECG from an abdominal signal. This monitor provides a noninvasive, continuous, real-time method of measuring instantaneous FHR and FHR beat-to-beat variability. This prototype system utilizes an Advanced Micro Device's 80186 microprocessor running at 10 MHz to perform the cancellation algorithm. It incorporates an 8-channel multiplier, sample-and-hold, and 12-bit 12 microsec. successive approximation analog-to-digital converter. Integrated with the microprocessor system are a 3-inch cathode ray tube and a 4.5-inch high-resolution thermal array printer to provide an immediate view and copy of the fetal heart rate and variability.

3. SUMMARY OF THE INVENTION

The proposed device consists of a flexible, multiconductor, ribbon type flat probe with an attached array of gold coated spherical electrodes. The entire assembly, except for a portion of each electrode is coated with an inert silicone insulator. It is designed to be inserted into the uterus at a time when a standard but invasive fetal scalp electrode would be applied. Following insertion the electrode array is scanned for electrode pairs which provide the best fetal ECG signal and which will usually include an interfering maternal ECG signal also. Other electrode pairs are scanned for component(s) of the interfering maternal ECG signal which do not include the fetal ECG signal. Both these signal sets are simultaneously derived and processed by the prior existing FHR monitor apparatus (U.S. Serial No. 61,575) to extract the fetal heart rate and variability data from

this ECG data. The device is designed as an alternative to the more invasive nature of the fetal scalp electrode and the less reliable methods of external fetal monitoring.

The direct fetal scalp spiral electrode is presently the most widely used device to accurately monitor the fetal heart rate. The intrauterine probe device described has the advantage that it would not penetrate the fetal scalp epidermis as the scalp electrode.

4. BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 depicts the intrauterine electrode array inserted in the uterus illustrating a large number of electrodes on both sides of a flat cable like structure used to collect the combined fetal and maternal ECG signal(s) from some electrode pairs and the maternal ECG signal(s) alone from different sets of electrode pairs separately.

Figures 2 through 5 are explodes drawings of the intrauterine electrode array based on the modification of a standard flexible, flat multiconductor, etched ribbon cable.

Figure 2 illustrates the electrical conductor aspect of the intrauterine array consists of a printed ribbon cable with a number of copper track conductors.

Figure 3 shows a design of a small number of ball electrodes attached to square conductive pads on a narrow ribbon cable.

Figures 4 and 5 illustrate steps in the assembly process of the intrauterine electrode array.

Figure 4 is an alternative design of the electrodes consisting of small spherical conductors.

Figure 5 illustrates an end view of the completed electrode array consisting of two of the assemblies in Figure 4 cemented back-to-back.

5. DESCRIPTION OF THE PREFERRED EMBODIMENT

Electrode Array Design

The general design of the fetal ECG electrode array is based on the fact that the fetal heart dipole orientation is not known and is likely to change during labor. The ability to automatically scan the length of a long asymmetric multi-electrode array will allow periodic adjustments in a 'near-continual' monitoring session. It should be noted that with certain hardware configurations it is, in principle, possible to continually monitor the fetal ECG, even as the selected electrode pairs change.

A key feature of this design is the ability to automatically scan many asymmetrically placed electrode pairs along both sides of the probe. Thus depending on the relative maternal and fetal cardiac dipoles, some electrode pairs will register fetal ECG only, maternal ECG only, or combined ECG signals.

The intrauterine electrode array design described will allow the reliable monitoring of the fetal heart rate and beat-to-beat fetal heart beat variability.

Detailed Mechanical Design

The design of the intrauterine electrode array is based on the modification of a standard flexible, flat multiconductor, etched ribbon cable. Such cables are available with numerous copper tracks on a thin mylar base. They are commonly used in

equipment where large numbers of conductors connect moving parts, e.g., print-heads etc.

The new design, is a novel utilization of readily available flexible ribbons on which the number and configuration of conductors is only limited by current printed circuit technology. Figure 1 shows the long flexibe intrauterine array that runs the entire circumference of the uterus. The drawing shows only a few of a large number of electrodes on both sides of the array. The large number of electrodes is included so that from both along its length and between both sides of its asymmetric construction a very large number of electrode pairs can be computer scanned to select two sets of ECG signals. The first signal set desired is a relatively large fetal ECG signals, which will usually contain same component of the maternal ECG signal. The second ECG signal set desired simultaneously from other electrode pairs is that signal set containing maternal ECG components alone without a fetal ECG signal. This second signal set is to be collected and later used to adaptively cancel the interfering maternal ECG signal from the first selected combined ECG signal. Figure 2 shows a simplified drawing of one such design. The electrode array will consist of a standard, printed ribbon cable. The number of conductors (copper tracks) can be chosen at will by cutting a wider ribbon with a straight-edge and razor blade. These cables are available in single or double-sided configurations and track widths, and can be special-ordered with different track patterns, connector terminations and even printed-through holes. They are also available as solid copper-

clad ribbons for 'in-house' track design and etching. This allows for a great deal of flexibility in design.

The electrodes themselves consist of gold-coated metal spheres which are attached to the ribbon tracks by conductive epoxy. The spheres are gold coated to produce a chemically inert surface since they will contact the uterus, placenta and fetus. The spheres are available in a variety of sizes and materials. The gold coating is applied by vacuum sputtering.

As Figure 3 shows, a simple preliminary design consisting of a small number of electrodes attached to a narrow ribbon cable (approx. 1 cm wide). An alternative design which utilizes much larger spherical electrodes on the same width cable is shown in Figure 4. Here all of the conductor tracks are made very narrow and are routed along one or both edges of the ribbon. At the appropriate distance each conductor is led to the center, where it terminates in a large pad. In this way it is possible to attach relatively large spherical electrodes in a linear array without interference with adjacent tracks.

Figures 4 and 5 illustrate the next steps in the assembly of the Intrauterine Electrode Array. The aim here is to insulate the entire assembly except for the outer hemispheric portion of the electrode spheres. The ribbon with the attached spheres is placed in a specially milled teflon trough of the appropriate length. The width of the trough is somewhat wider than the ribbon. Next the trough is flooded with self-leveling silicone rubber (GE RTV 118) so that the silicone completely coats the top surface of the ribbon to a thickness which leaves exposed the upper hemisphere of the sphere electrodes. (The ends of the

trough are appropriately dammed.) Twenty-four to 48 hours later the cured silicone rubber containing the ribbon electrode assembly is removed from the mold. Two of these assemblies (they may be differently configured) are then cemented back-to-back, the cement being the same RTV 118. The mylar ribbons and the overlapping silicone rubber edges are then held in proximity until the RTV cures.

The result is a double-sided, flexible electrode array of any desired configuration. A double sided electrode array not only increases the number of possible electrode combinations but also allows for the recording of signals such as the maternal ECG from regions directed away from the fetus. The connector-end track terminations are gold-plated for a short distance under the silicone so that the whole assembly can be chemical-sterilized. The stiffness of the assembly is controlled by incorporating any number of shims (mylar or plastic) between the two layers of the electrode array. An alternative would be to incorporate one or two angiographic catheters in the lateral edges of the assembly at the time of silicone potting. These catheters can then be used as guide-wire sheaths to stiffen the assembly at the time of insertion. Once the wires are removed the lumen can be used for intrauterine pressure monitoring or fluid infusion. The device will require a stiffness sufficient for intrauterine placement and yet have some compliance and flexibility to assure safety against uterine or placental perforation.

This device is connected to existing fetal heart rate monitoring equipment utilizing the abdominal ECG mode of

monitoring with adaptive digital filtering (U.S. Serial No. 61,575) which has previously been shown to be able to continually monitor fetal heart rate noninvasively, consistently and reliably, given an adequate fetal signal, such as the normal, term fetus at 42 weeks gestation. Electrode combinations are selected automatically by the FHR monitor computer so as to maximize the fetal ECG signal in one signal set and simultaneously obtain a second set of maternal ECG signals to adaptively cancel the appearance of any maternal ECG signal in the signal containing the relatively large fetal ECG signal. This can be achieved manually by switching various lead combinations while monitoring the ECG strip-chart output.

A predetermined sequence of electrode pairs will be selected for connection to the PMS fetal heart rate monitor through a patch-panel. The signal quality will be assessed using the built-in oscilloscope.

For the purpose of this description, we define beat-to-beat variability as the absolute difference between consecutive fetal ECG R-R intervals in units of beats per minute. Instantaneous FHR variability will be displayed on an expanded scale of the strip-chart record which overlaps the uterine activity trace. The use of this intrauterine array will lead to simpler and safer methods of testing fetal well-being both before and during labor. The conventional spiral electrode screwed into the fetal scalp has several potential risks: it can result in infection or permanent injury to the fetus; it is easily dislodged from the scalp; it can be mistakenly applied to improper sites on the fetus (e.g., face, fontanels, or genitalia). A fetal ECG

intrauterine catheter would not have these associated risks since it is placed in the uterine cavity without direct attachment to the fetus.

6. CLAIMS

What is claimed and desired to be secured by United States Letters Patent is:

1. An apparatus for monitoring instantaneous fetal heart rate and fetal heart rate beat-to-beat variability comprising:

a number of electrical means for independently receiving one set of electrical signals received through amniotic fluid transmitted from the heart of the mother and the fetus and

a different set of electrical means for independently receiving a second set of electrical signals received through amniotic fluid from the heart of the mother only for the purpose of cancelling or eliminating the maternal signal from the first received signal to obtain fetal heart rate.

7. DRAWINGS

Five drawing of the intrauterine electrode array are included as a part of the specification.

1/2

FIG. 1

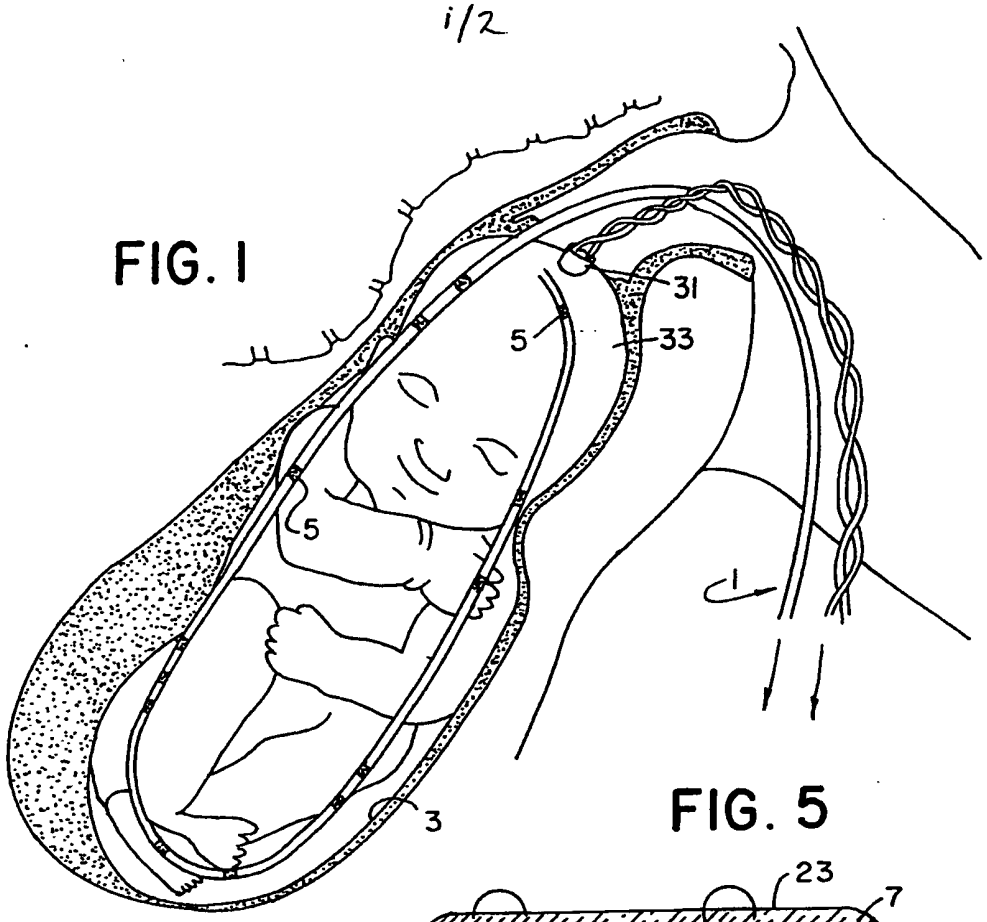
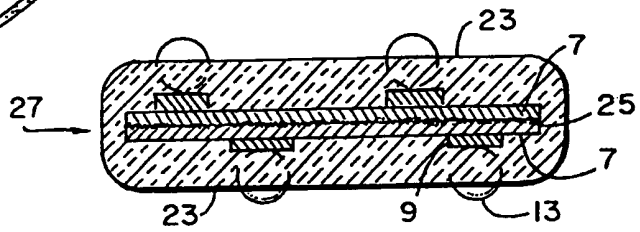


FIG. 5



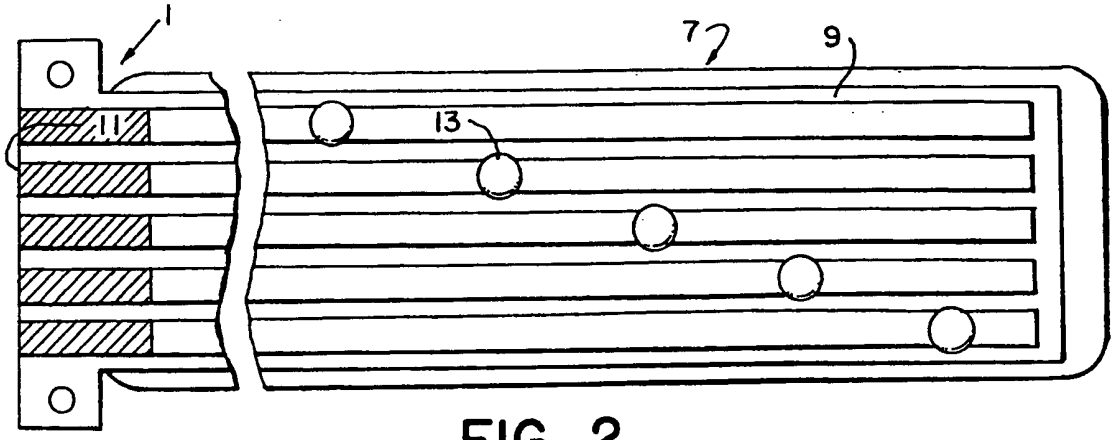


FIG. 2

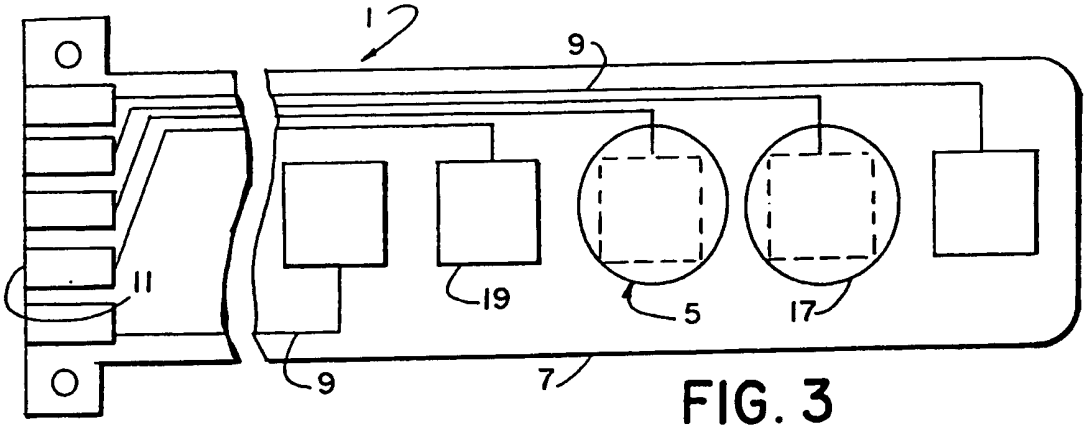


FIG. 3

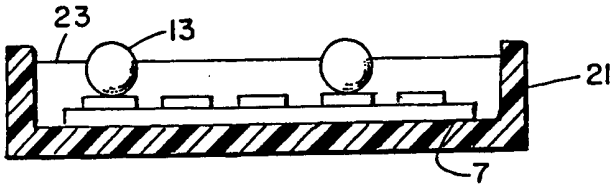


FIG. 4C

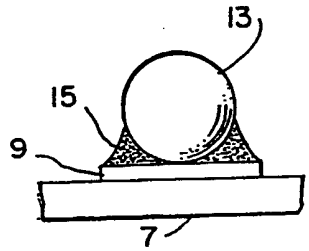


FIG. 4B

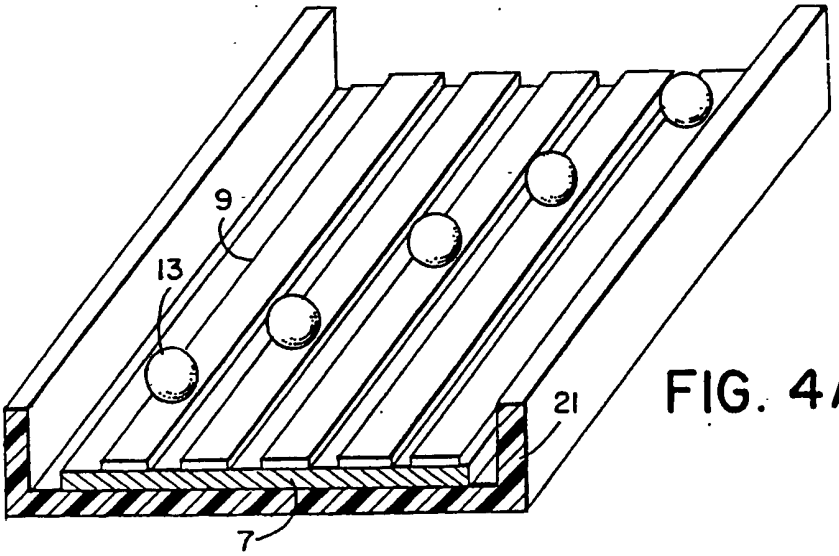


FIG. 4A

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US92/06967

A. CLASSIFICATION OF SUBJECT MATTER

IPC(5) :A61B 5/04
US CL :128/642, 698
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 128/639,641,642,644,698,784,798

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

none

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US,A, 5,025,787 (Sutherland et al.) 25 June 1991. See entire document.	1
X	GB,A, 2,195,897 (Sutherland et al.) 20 April 1988 (See entire document).	1

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be part of particular relevance

"E" earlier document published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
02 NOVEMBER 1992

Date of mailing of the international search report
05 JAN 1993

Name and mailing address of the ISA/
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231
Facsimile No. NOT APPLICABLE

Authorized officer
SAMUEL GILBERT
Telephone No. (703) 308-0858

Form PCT/ISA/210 (second sheet)(July 1992)*